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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,380	03/12/2004	Viia Valge-Archer	01997.043500	6499

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EXAMINER	
STOICA, ELLY GERALD	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/798,380	VALGE-ARCHER ET AL.	
	Examiner	Art Unit	
	ELLY-GERALD STOICA	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22, 24-39 and 40* is/are pending in the application.

4a) Of the above claim(s) *14,16-22 and 24-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13, 15, 38 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/30/2007 has been entered.

Status of the claims

Claims 1-22, 24-39 and the newly presented claim 40 are pending. Claims 1-7, 10 and 39 were amended and the claim 40 was presented. Claims 14, 16-22, 24-37 remain withdrawn being drawn to non-elected subject matter. Claims 1-13, 15 and 38-40 are currently being examined.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-13, 15 and 38-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the antibody of any of the claims 1-7 and 39-40 binds to what is referred in the claims as " an extracellular domain of a human or a mouse IL-21R". It is not clear if this refers to **the** extracellular domain of the respective receptors or to particular subsets of them or if there is only one extracellular domain present. Consequently, the metes and bounds of the claims 1-7 and 39-40 (and of the dependent claims 8-13, 15, and 38) could not be determined.

Claims 4 and 5 are indefinite for failure to identify an upper limit to the number of conservative substitutions. The metes and bounds of the claims could not be determined.

Claim 38 is indefinite because there is no relationship between the elements of the kit specified as for instance in the line of "wherein the antibody and the reagent are in separate containers".

Regarding claims 39 and 40 it is further unclear if the replacement of the CDRs or of the V_H or V_L portions of the antigen binding molecule is done by corresponding replacement (i.e. CD3 for CD3, but not CD1 for CD3)or not.

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2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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3. Claims 4 and 5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the claims are drawn to a genus of antibodies that comprise either a V_H or a V_L or conservative amino acid substitutions thereof.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the factors present in the claim is a functional requirement of binding to the extracellular domain of a human or a mouse Il-21R and the structural requirement of the conservative amino acid substitutions made in the CDRs of the respective antibodies. However there is no upper limit to the number of substitutions that can be made and if there are any non-substitutable residues that are absolutely necessary for binding of the receptor. Also there is no indication if the binding has to be to exactly the same epitope as the antibody having the disclosed CDRs. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Additionally, the description of an antibody having one V_H or V_L domain

does not constitute adequate written description of an entire genus of functionally equivalent antibodies which might comprise an undisclosed number of substitutions in its structure

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only antibodies comprising the disclosed CDR sequences but not the antibodies having and undisclosed number of substitutions but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim 39 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had

possession of the claimed invention. Specifically, the claim is drawn to an antibody that is produced by a method comprising:

(a) providing a repertoire of nucleic acids encoding a variable domain that either includes a CDR 1, 2 or 3 to be replaced or lacks a CDR 1, 2 or 3 encoding region;

(b) combining the repertoire with a donor nucleic acid encoding an amino acid sequence substantially as set forth in SEQ ID NOs: 68, 69, 70, 71, 72, or 73, such that the donor nucleic acid is inserted into the CDR 1, 2 or 3 region in the repertoire, so as to provide a product repertoire of nucleic acids encoding a variable domain;

(c) expressing the nucleic acids of the product repertoire;

(d) selecting an antibody or an antigen-binding fragment expressed from the product repertoire of nucleic acids, wherein the antibody or antigen-binding fragment is specific for an extracellular domain of a human or a mouse IL-21R.

With regard to the antibody definition, the definition offered by the applicant that an antibody "encompasses any polypeptide comprising the antigen binding site" (page 16, [0042]), where an antigen binding domain could be an isolated complementarity determining region (CDR), contravenes with the accepted state of the art which shows that the antibody specificity is conferred by at least five if not the full complement of six CDRs (figure 3.8, paragraph 3.6 as well as the Glossary, in chapter 3, Immunobiology, Janeway et al. eds., Garland publishing, New York, 2001, ISBN 081533642 X; also, US Pat. No. 5565332, col. 6, line 51-col. 7, line 11). In the Final rejection of 05/13/2007, the Examiner emphasized that the description of an antibody by less then three CDRs is considered inadequate. Reduction to practice in effect provides the only evidence to

corroborate conception (and therefore possession) of the invention. In the claim 39, it may be construed that an antibody fragment lacking a CDR 1, 2 or 3 encoding region might mean lacking all of them and the combining of the repertoire with a donor nucleic acid encoding an amino acid sequence of jus on or two CDRs would lead to an antibody having less than three distinctive CDRs. Therefore the claim lacks adequate written description.

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Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claim is drawn to an isolated antibody which binds the same epitope on a polypeptide with at least 85% identity to the polypeptide set forth in SEQ ID NO: 43 or

SEQ ID NO: 45, or a fragment thereof, an extracellular domain of a human or a mouse IL-21R as an antibody comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 65, 66, and 67. The state of the prior art was aware of the existence of interfering antibodies, as the antibody claimed is. However, the epitope(s) that dictate the binding may be contiguous or not. An interfering antibody as claimed might not need to bind to the entire epitope or not binding the epitope at al but very close (tridimensionally) to the epitope intended and thus block the steric access of the antibody having the V_H, the V_L or the scF_v sequence mentioned in the claim. This situation would lead a person of ordinary skill in the art to conclude that the antibody has actually bound to the epitope, since the binding of the epitope would be sterically hindered. It would take a good amount of experimentation to detect the situation that the antibody claimed binds exactly the same epitope with the antibody having the sequences mentioned. This is especially true since the specification does not provide any description or guidance with respect to the epitope bound by the antibody comprising an amino acid sequence selected from the group consisting of Seq. Id. Nos.: 65, 66 or 67. Therefore, due to the uncertainty with regard to the detection of an antibody that actually binds the epitope and not a mere interfering antibody, the lack of description of the epitope and of guidance of uncovering it, the amount of experimentation needed to obtain such an antibody is considered undue.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claim 39 rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hodge MR (WO200069880, 11/23/2000).

The claim is drawn to an antibody having certain disclosed CDRs, as presented supra. It may be construed that an antibody fragment lacking a CDR 1, 2 or 3 encoding region might mean lacking all of them and the combining of the repertoire with a donor nucleic acid encoding an amino acid sequence of just one or two CDRs would lead to an antibody having less than three distinctive CDRs.

Hodge MR claims (claim 11) an antibody that selectively binds to a polypeptide of SEQ ID NO 2 (that is the human IL-21 receptor). Hodge is silent about any particular CDRs. However, due to the breadth of the claims and since the specificity of the antibody is conferred by the CDR regions, it appears that the antibody of Hodge would have contained at least a number of the CDR regions enumerated in the instant

application and therefore anticipate or make obvious the antibody of the claims in the instant application.

Conclusion

7. No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to ELLY-GERALD STOICA whose telephone number is (571)272-9941. The examiner can normally be reached on 8:30-17:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lorraine Spector/, Ph.D.

Primary Examiner, Art Unit 1647